

**REMARKS**

Applicants respectfully request the Examiner to reconsider the present application and allow the pending claims in view of the foregoing remarks.

***Status of the Claims***

Claims 1-10, 14, and 15 are pending in the present application. No claims are being added, amended or canceled. Thus, a listing of the claims is not necessary.

***Issues under 35 U.S.C. § 103(a)***

Claims 1-7, 9 and 16-20 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over D. Allred et al. (*J. Natl. Cancer Inst.*, Vol. 85(3), pp. 200-206 (1993); hereinafter “Allred”) in view of U.S. Patent No. 5,527,676 (B. Vogelstein; hereinafter “Vogelstein ‘676”).

Also, claims 1, 3 and 10 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Allred in view of Vogelstein ‘676, further in view of Hedrum et al. (*Biotechniques*, Vol. 17(1), pp. 118-9, 122-4, 126-9 (1994); hereinafter “Hedrum”).

Further, 1, 2 and 19 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Allred in view of Vogelstein ‘676, further in view of Hollstein (*Science*, Vol. 253, pp. 49-53 (1991); hereinafter “Hollstein”).

Applicants respectfully traverse, and reconsideration and withdrawal of this rejection are respectfully requested.

One of ordinary skill in the art would not combine the cited references

Applicants respectfully submit that a *prima facie* case of obviousness has not been established. All outstanding rejections cite Allred in combination with Vogelstein '676. However, Applicants respectfully submit that one of ordinary skill in the art would not combine these two references, or further with Hedrum or Hollstein, in order to achieve what is instantly claimed for the reasons stated below.

The Examiner states what the deficiencies of the cited Allred reference are at page 4, lines 4-8 of the Office Action. However, these are significant deficiencies of Allred. Then, Vogelstein '676 is cited as a secondary reference to account for the deficiencies of Allred. Specifically, the disclosure of Vogelstein '676 is discussed followed by the conclusions or reasons of combining the references are given at, e.g., the paragraph bridging pages 5-6 of the Office Action. However, the mere fact that disclosures can be combined does not make the combination obvious unless the art also contains something to suggest the desirability of the combination. *See, In re Gordon*, 221 USPQ 1125, 1127 (Fed. Cir. 1984) and *In re Imperato*, 179 U.S.P.Q. 730, 732 (CCPA 1973).

Here, the conclusions in the Office Action of why Allred is combined with Vogelstein '767 are improper in that the mentioned suggested desirability is lacking. Allred et al. do not use a DNA diagnostic method in their article, wherein their approach is immunochemical. The Examiner then cites Vogelstein '676. However, there is no justification in referring to Vogelstein '676 for the nucleic acid analysis aspect. Applicants note that the nucleic acid analysis of Vogelstein '676 uses PCR with two primers (see column 5, line 62 to column 6, line 4). The amplified DNA is then usually analyzed by other techniques (e.g., blotting examples 1, 23).

Thus, the skilled artisan would understand that there is no description or recognition in the cited references that the entire nucleotide sequence of each DNA sample is determined by a sequencing method. Once the DNA from the tumor has been amplified, it is analyzed via a further technique, but that would not include sequencing. Thus, under *In re Gordon*, the skilled artisan would not have any desired suggestion to combine the disclosure in the two cited references of Allred and Vogelstein '676. Withdrawal of this rejection is respectfully requested.

Applicants add that while the reference need not expressly teach that the disclosure contained therein should be combined with another, *see Motorola, Inc. v. Interdigital Tech. Corp.*, 43 USPQ2d 1481, 1489 (Fed. Cir. 1997), the showing of combining references "must be clear and particular". *See In re Dembiczak*, 175 F.3d 994, 998, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999). Here, there is no such clear and particular guidance in any of the cited references to achieve the method as presently claimed. In other words, one of ordinary skill in the art would not be motivated, and/or reasonably expect to be successful, in combining Allred with Vogelstein '676 to achieve what is instantly claimed since there is no disclosure of, e.g., the entire nucleotide sequence is determined by a sequencing method in either reference. Thus, the instant rejections are improper (all 3 rejections cited Allred and Vogelstein '767).

Also, the sentence bridging pages 5-6 of the Office Action appears to account for the requisite reasonable expectation of success (one of three requirements for a *prima facie* case of obviousness). *See In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). However, Applicants respectfully that this conclusion is improper since "Obviousness requires one of ordinary skill in the art have a reasonable expectation of success as to the invention—'obvious to try' and 'absolute predictability' are incorrect standards." *Velander v. Garner*, 68,

USPQ2d 1769, 1784 (Fed. Cir. 2003) (citing *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673 (Fed. Cir. 1988)). The conclusion in the Office Action amounts to an improper “obvious to try” rationale. Further, just because Allred et al. recognize some important mutations in p53 does mean the skilled artisan would have the required level of reasonable expectation of success. As stated in Applicants’ specification at page 3, lines 33-37, the state of the art is such that there is no correlation with the p53 mutations and clinical parameters and prognosis in other respects. Further, Allred makes no reference to using a nucleotide sequence, such as that disclosed in Vogelstein ‘676. Further, Vogelstein ‘676 uses PCR with primers. And again, Examiner states what the deficiencies of the cited Allred reference are at page 4, lines 4-8 of the Office Action, but Applicants submit that these are significant deficiencies of the primary reference. In addition, Vogelstein ‘776 cannot properly account for such big deficiencies in Allred as discussed above.

With regard to the other rejections further citing either Hedrum or Hollstein, such combinations are also improper for the same reasons discussed above. Adding the disclosure of either reference does not make the combination as Allred and Vogelstein ‘767 as proper.

Thus, Applicants respectfully submit that a *prima facie* case of obviousness has not been established with respect to all rejections, and request withdrawal thereof.

### ***Conclusion***

A full and complete response has been made to all issues as cited in the Office Action. Applicants have taken substantial steps in efforts to advance prosecution of the present

application. Thus, Applicants respectfully request that a timely Notice of Allowance issue for the present case.

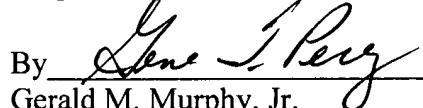
Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three (3) month extension of time for filing a reply in connection with the present application, and the required fee of \$1020.00 is attached hereto.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Eugene T. Perez (Reg. No. 48,501) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

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